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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,728	07/03/2001	John F. Wironen	RTI-133	8170

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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/897,728	WIRONEN ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005 and 10 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-23,31 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-23,31 and 37* is/are rejected.

7)☒ Claim(s) *3* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments and remarks, filed 5/5/05 and 1/10/05, are acknowledged. Amended claims 1, 3-4, 10-11, 13-14, 16-19, 23, and 31; new claim 37; and cancelled claims 2, 24-30, and 32-36 are acknowledged.

Applicant's arguments, filed 5/5/05 and 1/10/05, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1, 3-23, 31, and 37 are herein under examination.

Claim Objections

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 currently depends from a cancelled claim. However, for the remainder of this office action and current prosecution, instant claim 3 is interpreted as if it depends from instant claim 1. This objection is necessitated by amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-22, 31, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following phrases do not appear to have written support in the specification, claims, or drawings, as originally filed: "does not require [...] use of cell-based assays" (claim 1, lines 8-9) and "less than *about* 3 percent" (claim 4, lines 3-4). While the abstract recites not needing in vivo assays and the specification recites in vitro cell-based assays (page 4, last paragraph to page 5, first paragraph), it fails to recite that the use of cell-based assays is not required. It is noted that negative limitations must have written support just as positive limitations in a claim must have written support. While the specification recites calcium content less than 3% (page 17, line 22), it fails to recite calcium content less than about 3% which differs in scope. Because the introduction of phrases "does not require [...] use of cell-based assays" (claim 1, lines 8-9) and "less than *about* 3 percent" (claim 4, lines 3-4) do not appear to have adequate written support in the specification, claims, or drawings, as originally filed, they are considered to be NEW MATTER. Claims 5-22, 31, and 37 are also rejected due to their direct or indirect dependency from claims 1 and 4. This rejection is necessitated by amendment.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

These rejections are necessitated by amendment.

Claim 3 recites the limitation "said bone implant material" in line 1. There is insufficient antecedent basis for this limitation in the claim as there is no prior mention of this phrase, because this claim depends from cancelled claim 2. This rejection would be nullified if claim 3 was amended to depend from claim 1. Claims 4-11 are also rejected due to their direct or indirect dependency from instant claim 3. This rejection is necessitated by amendment.

Claim 1 recites the phrase "like implant materials comprising bone" (lines 2 and 5) which is indefinite because it is unclear what is "like" implant materials comprising bone. Does this mean they are all "like" bone? It is possible that Applicant intends the phrase to mean that the materials are "alike"; however, this is not clear in the amended changes to this limitation.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6, 19-20, 22-23, 31, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al. (Journal of Periodontology, 1997 Nov; Vol. 68(11), pages 1076-1084).

This rejection is necessitated by amendment.

Zhang et al. disclose an in vitro method for quantifying the osteoinductive potential of demineralized bone matrix (a collection of like implant material) from cadaverous humans before clinical (human) use (allograft) (title; abstract; page 1077, col. 2, second paragraph), as stated in instant claims 1 and 23. Zhang et al. disclose exposing ground bone (implant material) to dilute hydrochloric acid, a demineralization process to dissolve the bone material (page 1077, col. 1, last paragraph to col. 2, first paragraph) as stated in instant claims 4 and 5. Zhang et al. disclose calcium content of bone being demineralized can be demonstrated to be a linear function of pH of the solution (abstract and page 1077, col. 2, first paragraph) as well as calcium content determination (page 1077, col. 2, last paragraph to page 1078, col. 1, first paragraph) with the positive presence of calcium (abstract and Figures 1, 3, 4). Figure 3 shows calcium content less than 3%, as stated in instant claim 4. Zhang et al. disclose the bone matrices being separated into particles according to size ranges with sieves (page 1077, col. 1, last paragraph). Zhang et al.

disclose combining bone cells with EDTA and trypsin (enzyme) (page 1078, col. 1, third paragraph) which represents dissolving the bone implant matrix with an enzyme, as stated in instant claim 6. Trypsin is utilized and then ALP was measured (page 1078, col. 2, first paragraph) which represents an enzyme that did not destroy osteoinductive factors present in the releasate, as stated in instant claim 6. Zhang et al. disclose quantifying the concentration of alkaline phosphatase (ALP) (implant material releasant of osteogenic factor) via a protein assay using milligram quantities (page 1078, col. 1, last paragraph to col. 2, first paragraph) as stated in instant claims 1, 19, and 23. Zhang et al. disclose mesenchymal cell induction process (morphogenic) is frequently monitored by changes in ALP activity of cells being studied (page 1081, col. 1, second paragraph). Zhang et al. disclose changes in ALP level with time were studied to assess effects of DBM on human periosteal cell induction (page 1081, col. 1, second paragraph). Zhang et al. disclose noting changes in ALP concentration on curves with noted values of DBM to determine osteogenic potential of implant material (Figures 6 and 7) which represents converting concentration values of an osteogenic factor to an osteogenic potential for a representative sampling, as stated in instant claims 1 and 23. The control curve in Figure 6 represents a predetermined curve, as stated in instant claims 1 and 23. Zhang et al. disclose osteoinductivity of demineralized bone matrix is due to bone morphogenetic proteins (BMPs) and other noncollagenous proteins in the matrix (page 1077, col. 1, third paragraph). Zhang et al. disclose proliferation effects of demineralized bone matrix were studied to assess potential mitogenic effects (page 1080, col. 2, second paragraph). Zhang et al. disclose a correlation graph between in vitro of ALP activity (concentration) and percent calcium (probability to generate bone in vivo) (Figure 8), as stated in instant claim 20. Zhang et al. disclose using periosteal cells

which are presumed to be responsive to BMPs actions, differentiating into osteoblast cells and correlations with ALP (Figure 8 and page 1083, col. 1, third and fourth paragraphs), as stated in instant claim 22. Zhang et al. disclose the in vitro assay may be a good substitute for the in vivo assay in assessing osteoinductive potential of demineralized bone matrix and reduce animal use via quality assessment of produced bone products (select bone material) for clinical application (to be implanted into patient) (page 1083, col. 1, last paragraph to col. 2, first paragraph), as stated in instant claim 31. Zhang et al. disclose that in vitro ALP activity peaks on day 5 and the in vitro assay requires only 1 week to obtain information regarding osteoinductive potential of demineralized bone products (page 1083, col. 2) which represents a total time of less than about 4 days with the word "about" being interpreted broadly, as stated in instant claim 37. Zhang et al. disclose calcium contents are used as a major indicator of osteoinductivity (page 1082, col. 2, third paragraph) and Figure 8 demonstrates correlations between calcium and ALP (in vitro).

Thus, Zhang et al. anticipate the limitations in claims 1, 3-6, 19-20, 22-23, 31, and 37.

Applicants argue that osteogenic factors are described in the specification (page 6, lines 6-8) as "mammalian bone matrix-derived proteins which exhibit the ability to promote or stimulate local osteogenesis at sites of implantation in mammals. This statement is found unpersuasive as the specification on page 6, lines 4-5, recite "human-derived osteogenic factors" and on line 6 states the invention is directed to "mammalian bone matrix-derived proteins...". These two sentences do not clearly and concisely provide a definition of osteogenic factors, therefore the phrase is to be interpreted broadly and reasonably to encompass any factor involved in an osteogenic manner; in other words, producing or originating in bone.

Applicants argue that Zhang et al. do not directly measure an osteogenic factor, but rather indirectly measures osteogenic activity by measuring the enzyme alkaline phosphatase (ALP). This statement is found unpersuasive as the instant claims do not recite any limitation regarding direct or indirect measurements. Applicants argue that ALP is not an osteogenic factor, since it does not directly promote or stimulate osteogenesis. It is noted that osteogenic can be interpreted broader than Applicants have just cited, as seen in the last line of the previous paragraph.

Applicants argue Zhang et al. loosely correlate calcium production to ALP concentrations. This statement is found unpersuasive as Zhang et al. disclose calcium contents are used as a major indicator of osteoinductivity (page 1082, col. 2, third paragraph) and Figure 8 demonstrates correlations between calcium and ALP (in vitro). Applicants argue that Zhang et al. do not disclose directly measuring bone growth factors nor converting the concentration of those factors directly to osteoinductivity. These statements are found unpersuasive as the instant claims do not recite direct measurements. In addition, indicators as described on page 1082 (col. 2, third paragraph) and correlations in the Figures provide ample evidence of conversion data. Applicants disclose differences in correlation percentages of the Zhang et al. reference and the instant invention; however, this is found unpersuasive as these limitations are not recited in the instant claims. Applicants argue that instant claims 1 and 23 require avoiding the use of "cell-based assays". This statement is found unpersuasive as the claims do not require avoiding the use of cell-based assays, but rather the quantifying does not require the use of cell-based assays. This is interpreted to mean that it does not matter if cell-based assays are used. Applicants argue that the instant invention does not require the use of living test animals or cell cultures. While the invention does not require these entities, the instant claims recite open claim language, thus

use of cell-based assays, cultures and/or animals are not precluded. Applicants' arguments are deemed unpersuasive for the reasons given above.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

MARJORIE A. MORAN
PRIMARY EXAMINER

July 11, 2005

Marjorie A. Moran
7/18/05